Art 34 AMD

WHAT IS CLAIMED

Sub Q5

1. A non-human mammal comprising a mutant GP IIIa gene wherein at least one of the two cytoplasmic tyrosine residues encoded by the gene has been replaced with a non-tyrosine residue.

2. The non-human mammal of claim 1 wherein the non-tyrosine residue is phenylalanine.

3. The non-human mammal of claim 1 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

4. Platelets isolated from the blood plasma of the non-human mammal of claim 1.

5. The non-human mammal of claim 1 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

6. The non-human mammal of claim 5 wherein the non-human mammal is a mouse.

7. The non-human mammal of claim 1 wherein both cytoplasmic tyrosine residues have been replaced with a non-tyrosine residue.

8. The non-human mammal of claim 7 wherein the non-tyrosine residues are phenylalanine.

9. The non-human mammal of claim 7 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

10. Platelets isolated from the blood plasma of the non-human mammal of claim 7.

11. The non-human mammal of claim 7 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

12. The non-human mammal of claim 11 wherein the non-human mammal is a mouse.

13. A non-human mammal expressing a transgene stably introduced into its DNA, wherein the transgene comprises DNA encoding mutant GP IIIa wherein at least one of the two cytoplasmic tyrosine residues has been replaced with a non-tyrosine residue.

14. The non-human mammal of claim 13 wherein the non-tyrosine residue is phenylalanine.

15. The non-human mammal of claim 13 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

16. Platelets isolated from the blood plasma of the non-human mammal of claim 13.

17. The non-human mammal of claim 13 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

18. The non-human mammal of claim 17 wherein the non-human mammal is a mouse.

19. The non-human mammal of claim 13 wherein both cytoplasmic tyrosine residues have been replaced with a non-tyrosine residue.

20. The non-human mammal of claim 19 wherein the non-tyrosine residues are phenylalanine.

21. The non-human mammal of claim 19 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

22. Platelets isolated from the blood plasma of the non-human mammal of claim 19.

23. The non-human mammal of claim 19 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

24. The non-human mammal of claim 23 wherein the non-human mammal is a mouse.

25. A method of preparing a transformed non-human mammal with a mutant GP IIIa gene wherein at least one of the two tyrosine residues encoded by the endogenous GP IIIa gene has been replaced with a non-tyrosine residue to prepare the mutant GP IIIa, said method comprising:

a) introducing into embryonic stem cells a nucleic acid molecule encoding the mutant GP IIIa gene;

b) regenerating a transformed non-human mammal from the cells resulting from step a).

26. The method of claim 25 wherein the non-tyrosine residue is phenylalanine.

27. The method of claim 25 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

28. The method of claim 25 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

29. The method of claim 28 wherein the non-human mammal is a mouse.

30. The method of claim 25 wherein both cytoplasmic tyrosine residues have been replaced with a non-tyrosine residue.

31. The method of claim 30 wherein the non-tyrosine residues are phenylalanine.

32. The method of claim 30 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

33. The method of claim 30 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

34. The method of claim 33 wherein the non-human mammal is a mouse.

35. The method of claim 25 further comprising breeding the transformed non-human mammal so as to produce a non-human mammal homozygotic for the mutant GP IIIa gene.

36. The method of claim 35 wherein the non-human mammal is a mouse.

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37. A method of preparing a transformed non-human mammal with a mutant GP IIIa gene wherein at least one of the two tyrosine residues encoded by endogenous GP IIIa gene has been replaced with a non-tyrosine residue to prepare the mutant GP IIIa, said method comprising:

a) introducing into embryonic stem cells a nucleic acid molecule encoding the mutant GP IIIa gene and a selectable marker flanked by FRT sites;

b) identifying and selecting transformed cells;

c) removing the selectable marker from the transformed cells selected in step b) by transient transformation with FLP recombinase;

d) injecting the transformed cells from step c) into blastocysts; and,

e) regenerating a transformed non-human mammal from the blastocysts of step d), wherein the regenerated transformed non-human mammal is chimeric for the mutant GP IIIa gene.

38. The method of claim 37 wherein the non-tyrosine residue is phenylalanine.

39. The method of claim 37 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

40. The method of claim 37 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

41. The method of claim 37 wherein the non-human mammal is a mouse.

42. The method of claim 37 wherein both cytoplasmic tyrosine residues have been replaced with a non-tyrosine residue.

43. The method of claim 37 wherein the non-tyrosine residues are phenylalanine.

44. The method of claim 37 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

45. The method of claim 43 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

46. The method of claim 45 wherein the non-human mammal is a mouse.

47. The method of claim 37 further comprising breeding the transformed non-human mammal so as to produce a non-human mammal homozygotic for the mutant GP IIIa gene.

48. The method of claim 47 wherein the non-human mammal is a mouse.

49. The method of claim 37 further comprising the following steps:

f) breeding the chimeric non-human mammal with a wild-type non-human mammal to produce a non-human mammal heterozygotic for the mutant GP IIIa gene;

g) crossing a heterozygotic non-human mammal produced in step f) with a second heterozygotic non-human mammal produced in step f); and,

h) selecting a non-human mammal homozygotic for the mutant GP IIIa gene from the resulting progeny.

50. The method of claim 49 wherein the non-human mammal is a mouse.

51. A method of determining the importance of phosphorylation in platelet function comprising comparing a characteristic mediated by platelet function, between two mammals of the same species, wherein one mammal has a wild-type GP IIIa gene and the other mammal has a mutant GP IIIa gene, wherein at least one of the two tyrosine

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residues encoded by the wild-type GP IIIa gene has been replaced with a non-tyrosine residue encoded by the mutant GP IIIa gene.

52. The method of claim 51 wherein the non-tyrosine residue is phenylalanine.

53. The method of claim 51 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

54. The method of claim 51 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

55. The method of claim 54 wherein the non-human mammal is a mouse.

56. The method of claim 51 wherein both cytoplasmic tyrosine residues have been replaced with a non-tyrosine residue.

57. The method of claim 56 wherein the non-tyrosine residues are phenylalanine.

58. The method of claim 56 wherein the cytoplasmic tyrosine residues are tyrosine residues 747 and 759.

59. The method of claim 56 wherein the non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

60. The method of claim 59 wherein the non-human mammal is a mouse.

61. The method of claim 51 further comprising comparing the bleeding time between the two mammal types.

62. The method of claim 51 further comprising comparing the thrombotic responses between the two mammal types.

63. The method of claim 51 further comprising comparing angiogenesis between the two mammal types.

64. The method of claim 51 further comprising comparing tumor metastasis between the two mammal types.

65. The method of claim 51 further comprising comparing inflammation between the two mammal types.

66. The method of claim 51 wherein the mammal is a mouse.

67. A method of determining the effect of an agent on a characteristic of a mammal that is attributable to the expression of the GP IIIa gene, said method comprising;

a) administering said agent to the mammal of claim 1;
b) maintaining said mammal for a desired period of time after said administration; and,
c) determining whether a characteristic of said mammal that is attributable to the expression of the mutant GP IIIa gene has been affected by the administration of said agent.

68. The method of claim 67 wherein the mammal is a mouse.

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